Adrian Thrasher, a personal reflection from London:

While happily training as a respiratory doctor in London, an eminent physician at the Royal Brompton Hospital came back from a meeting in the US and reported on an idea to treat cystic fibrosis using adenoviruses. The thing that puzzled him most was the fact that our immune system would surely eliminate the therapy. Even so I found the concept intriguing, and it stuck in the back of my mind for some time. Later, and further on in my clinical training, I was somewhat reluctantly hauled into the lab by Professor Tony Segal FRS to work on an enzyme system in phagocytes responsible for efficient microbial killing. It had been worked out that defects in this complex caused a severe inherited immunodeficiency called Chronic Granulomatous Disease. The realisation that basic scientific enquiry could lead to elucidation of disease mechanisms, and therefore to the design of novel therapies set me on a completely new path as an academic clinician. During my PhD I showed for the first time in 1992 that the NADPH-oxidase could be corrected in vitro by retrovirus-mediated gene transfer, and at that point I entered a relatively nascent international gene therapy community. Soon after, I joined a pioneering bone marrow transplanter, Professor Roland Levinsky at the Institute of Child Health who had a vision that gene therapy would one day become a standard of care for many diseases. Early on he sent me on a trip to Palo Alto where a biotech company was beginning to explore the use of AAV for gene transfer. While I struggled to show anything meaningful in haematopoietic cells, it sparked a wonderful collaboration with Professor Robin Ali (current President ESGCT) culminating in one of the first clinical trials of gene therapy for an inherited blinding disorder, Leibers congenital amaurosis. When I started at The Institute of Child Health, I was fortunate to team up with Roland's clinical fellow and PhD student Professor Bobby Gaspar who became a long-term colleague and friend. From scratch, we built a centre for gene therapy of inherited immunodeficiencies, recruiting our first patient with X-linked SCID in 2001, and since have treated more than 60 with a number of different diseases. Of course, over the last 30 years the field has faced difficulties, but alongside remarkable clinical progress and success, and today we are entering an era where gene therapy is becoming part of mainstream medicine. At Great Ormond Street Hospital for Children, we are now trialling gene addition and recently editing for inherited immunodeficiency, metabolic, and neuromuscular conditions, and increasingly for haematological malignancy. Perhaps most satisfying for me is that we are finally beginning to see real clinical benefit for patients with CGD, the disease that I worked on at the beginning of my career. I have been privileged along the way to work and collaborate with some exceptional scientists and clinicians many of whom have become good friends. I was particularly proud to receive the ESGCT outstanding achievement award in my home-town of Brighton in 2011, and continue to enjoy working with the board and on the educational initiatives established for training of young scientists. Most of all I have total respect for the families and patients who have participated in the development of these pioneering therapies, as without their courage and belief we would not be where we are today.